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10/582,728	06/14/2006	Alberto Osio Sancho	O0327.70000US00	4669

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EXAMINER	
SHEIKH, HUMERA N	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,728	OSIO SANCHO, ALBERTO	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27,39,41-46 and 50-53* is/are pending in the application.

4a) Of the above claim(s) *4-7,15,17,25-27,39,41-46 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8-14,16,18-24 and 51-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/24/10; 12/01/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt is acknowledged of the Response, Amendment and Applicant's Arguments/Remarks, all filed 11/24/10 and the Information Disclosure Statements (IDS) filed 11/24/10 and 12/01/10.

Applicant has overcome the following objection(s) and/or rejection(s) by virtue of the amendment to the claims and/or persuasive remarks: (1) The claim objection for claim 21 has been withdrawn and (2) The 35 U.S.C. 102(b) rejection of claims 1-3, 8, 9, 11-13, 18, 22 and 23 over Harris et al. (EP 0 608 341) has been withdrawn.

Claims 1-27, 39, 41-46 and 50-53 are pending in this action. Claims 1-4, 12-15, 21, 39, 41-46 and 50 have been amended. New claims 51-53 have been added. Claims 4-7, 15, 17, 25-27, 39, 41-46 and 50 remain withdrawn (based on nonelected invention). Claims 28-38, 40 and 47-49 have been cancelled. Claims 1-3, 8-14, 16, 18-24 and 51-53 are currently under consideration. Claims 1-3, 8-14, 16, 18-24 and 51-53 remain rejected.

* * * * *

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 11/24/10 and 12/01/10 were filed after the mailing date of the Non-Final Office Action on 07/07/10. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

* * * * *

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12, line 3, recites the limitation "...consisting of other enzymes, anesthetics...". The term "other" renders the claim indefinite as to which particular additional enzymes Applicant is making reference to, asides from the ones recited in the generic claims (i.e., claims 1-3 which recite hyaluronidase, collagenase). The term "other" renders the claim vague and ambiguous as to which additional specific enzymes are required or suitable.

* * * * *

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 8-14, 16, 18-24 and newly added claims 51-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris et al. (hereinafter "Harris" (EP 0 608 341) in view of Marmo et al. (hereinafter "Marmo") (U.S. Pat. Appln. Publn. No. 2005/0080484) and further in view of Karageozian et al. (hereinafter "Karageozian") (U.S. Pat. No. 6,610,292).

Harris ('341) teaches methods for accelerated corneal reshaping involving the release of enzymes, particularly hyaluronidase, or other agent which facilitate reshaping of the cornea to reduce or eliminate refractive errors of the eye (page 2, lines 3-5). (This reads on Applicant's method for treating ophthalmologic conditions). The methods employ a contact lens for delivering agents to the eye and utilize hyaluronidase for the manufacture of a medicament for the treatment of refractive errors of the eye. An agent that softens the cornea of a mammalian eye for use in correcting refractive errors is also disclosed. The agent can be provided in combination with a rigid contact lens. The medicament may further comprise an anesthetic (p. 3, lines 13-38). The medicaments permit a method of reshaping a cornea from a first configuration to a second desired configuration in order to correct refractive errors in an eye (p. 3, line 39 – p. 4, line 5). The lens is removed when the cornea is capable of maintaining the desired second configuration without the support of the lens (p. 5, lines 8-9). The corneal agent(s) such as enzymes and enzyme activators can be administered in the form of eye drops (p. 4, lines 6-21). Where the corneal softening agent used is hyaluronidase, the inhibitor can be a hyaluronidase

inhibitor such as cysteine and EDTA. Collagenase is also disclosed (p. 4, lines 34-42). The primary enzyme used to soften a cornea is hyaluronidase (p. 6, line 32).

Harris does not teach the polymer of claim 14 (i.e., cellulose) and the ophthalmologic condition to be presbyopia of claim 24.

Marmo ('484) teaches methods and devices for improving vision comprising a corrective ocular device, such as a corneal appliance that is placed over an eye and has a lens body (see Abstract); (p. 1, ¶s 0003, 0009). The lens may be structured to correct visual deficiencies including myopia, hyperopia, astigmatism and presbyopia (p. 4, ¶ 0065). The lens includes a gel having at least one water soluble or water swellable polymeric material, for example at least one cellulosic component (i.e., hydroxymethyl cellulose and the like) and/or one or more other water soluble or water swellable polymeric materials (p. 10, ¶s 0108-0109); (p. 11 ¶ 0115).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to treat ophthalmologic conditions such as presbyopia and to incorporate the cellulosic polymeric materials as taught by Marmo within the methods of Harris. One would do so with a reasonable expectation of success because Marmo teaches methods to correct visual deficiencies, including presbyopia, which comprises providing a corrective ocular device, such as a corneal lens, whereby the lens includes suitable polymeric materials, such as cellulosic components (i.e., hydroxymethyl cellulose). The expected result would be an enhanced method for improving vision disorders and conditions.

With regards to the duration that the correction of the ophthalmologic condition lasts, as in claims 19-21, the references are silent as to this aspect. However, it would be reasonably expected that the duration of treatment that results from correction would last for an extended

period of time, in view of the fact that the prior art of record teaches the same methods and utilizes the same techniques as employed by the Applicant. The prior art clearly recognizes and teaches application of enzymes to contact lens to effectively treat ocular conditions (i.e., presbyopia) and thus employs treatment methods as claimed. Hence, the duration that the correction of the ophthalmologic condition lasts would reasonably be expected to be for an extended period of time (i.e., 1 year).

Harris and Marmo do not teach the hyaluronidase and collagenase.

Karageozian ('292) teaches a method for treating ophthalmic disorders of the mammalian eye using hyaluronidase (see column 4, lines 17-50, col. 5, lines 38-46 and Abstract). Karageozian teaches that the use of hyaluronidase as well as alternative enzymes are contemplated in the invention. Such enzymes include collagenases that can be used in the ocular treatment methods of Karageozian (col. 17, lines 29-40). The enzymes of the invention may be administered by suitable routes of administration (e.g., topically). See column 6, lines 43-50. While the combination of both hyaluronidase and collagenase is not explicitly taught, the reference does teach that one of skill in the art would select an appropriate enzyme and its dosage to practice the methods of the invention. In addition, the preparation provides for optimal therapeutic effects without causing ocular toxicity (column 17, lines 41-51).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ enzymes such as hyaluronidase or collagenase (or alternatively, combinations thereof) in the treatment of ophthalmologic conditions as taught by Karageozian within the methods of Harris. One would do so with a reasonable expectation of success because

Karageozian teaches methods for treating ophthalmic disorders, which comprises the use of hyaluronidase and alternative enzymes (collagenase) which are suitable for use in that they bring about optimal therapeutic effects without causing ocular toxicity (column 4, lines 17-21). The expected result would be an enhanced method for improving vision disorders and conditions.

This rejection is maintained and applied to newly added claims 51-53. Harris, as noted above, teaches methods for accelerated corneal reshaping involving the release of enzymes, particularly hyaluronidase, or other agent which facilitate reshaping of the cornea to reduce or eliminate refractive errors of the eye (page 2, lines 3-5). The method of administration includes the use of rigid contact lenses (as shown in Figs. 1-2), which are made from known fluoro silicone acrylate lens materials, which are gas permeable. See page 10, paragraph [0066]. Thus, this teaching meets the limitation of new claim 51. Harris teaches that their medicament is in the form of eye drops (see claim 2, page 17 of Harris). While Harris does not teach a "gel", note that the secondary reference of Marmo discloses that their lens includes a gel having at least one water soluble or water swellable polymeric material, for example at least one cellulosic component (i.e., hydroxymethyl cellulose and the like) and/or one or more other water soluble or water swellable polymeric materials (p. 10, ¶s 0108-0109); (p. 11 ¶ 0115) and thus meets new claim 52. With respect to new claim 53, the limitations therein are met by the combination teachings of Harris, Marmo and Karageozian, which recognize and teach treatment methods for presbyopia (see Marmo p. 4, ¶ 0065) and teach application of various enzymes including hyaluronidase and collagenase (see Harris and Karageozian). Thus, given the teachings of the combined references, the instant invention would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

* * * * *

Response to Arguments

Applicant's arguments filed 24 November 2010 have been fully considered and were found to be partially persuasive.

- **Claim Objections:**

Applicant argued, "Applicant has amended claim 21 to correct typographical errors, for example 'years' to 'year'."

This was persuasive based on the amendment to claim 21. Accordingly, the claim objection for claim 21 has been withdrawn.

- **Rejection under 35 U.S.C. 102(b) over Harris et al. (EPO 0608341):**

Applicant argued, "The Examiner points to page 4, lines 34-42, as specifically teaching use of collagenase, but nowhere in that section is collagenase mentioned. Harris, in fact, refers to collagenase only once, and only in the context of specifically dissuading one from using that enzyme (paragraph [0087] of Harris). Harris points only to matrix metalloproteinase-1 and matrix metalloproteinase-2 as corneal softening agents useful in breaking down collagen in the cornea (paragraph [0022] and page 7, Table II, of Harris). It is clear from the Applicant's specification that the term "collagenase" as claimed does not encompass these two enzymes (page 24, lines 24-31 to page 25, lines 1-2, of the Application as originally filed). Applicant amends the pharmaceutical composition recited in claims 1 to 3 to comprise an effective amount of hyaluronidase and collagenase. Since Harris does not teach the combination of hyaluronidase and collagenase, Harris does not anticipate amended claims 1-3, 8, 9, 11-13, 18, 22, and 23. Applicant respectfully requests that this rejection under § 102 be withdrawn."

Applicant's arguments have been fully considered and were found to be persuasive. Accordingly, the 35 U.S.C. 102(b) rejection of claims 1-3, 8, 9, 11-13, 18, 22 and 23 over Harris et al. (EP 0 608 341) has been withdrawn.

- **Rejection under 35 U.S.C. 103(a) over Harris et al. (EPO 0608341) in view of Marmo (US Pat. App. Pub. No. 2005/0080484):**

Applicant argued, "Harris does not teach the use of a polymer in the formulation or the treatment of presbyopia. The Examiner cites Marmo to remedy this deficiency in Harris. Applicant submits that one skilled in the art, seeking to improve upon the teachings of Harris, would not look to Marmo for guidance. Harris is directed to the field of enzyme orthokeratology, i.e., a non-surgical technique using a combination of contact lenses and enzymes for corneal reshaping to reduce or eliminate refractive errors of the eye. Marmo has nothing to do with enzyme orthokeratology and, in fact, does not teach the use of enzymes for correcting refractive errors of the eye. Marmo merely teaches a surgical technique involving cutting a "flap" or "pocket" beneath the epithelium of the cornea wherein a lens is inserted. The "gel" and "watersoluble or water swellable polymeric material" of Marmo described in paragraphs [0108] and [0109] is used to more effectively separate the epithelium of the cornea from Bowman's membrane prior to placement of the lens. The surgically implanted lens of Marmo may be a "vision correcting lens" to treat visual deficiencies. There is simply no motivation to combine the two references. One skilled in the art, seeking to improve on the non-surgical method of Harris, would certainly not be led to a reference which describes surgical methods, let alone motivated to combine the two to arrive at the presently claimed invention. The fact that Marmo teaches use of a polymer and treatment of presbyopia is irrelevant considering both of these features are involved in the placement of or use of a surgically implanted lens."

Applicant's arguments have been fully considered but were not found to be persuasive. In response to applicant's argument that there is no teaching, suggestion, or motivation to combine the references, the examiner recognizes that obviousness may be established by combining or

modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988), In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992), and KSR International Co. v. Teleflex, Inc., 550 U.S. 398, 82 USPQ2d 1385 (2007). In this case, while the primary reference of Harris does not teach the particular polymer(s) and the ophthalmologic condition to be treated – presbyopia, the secondary reference of Marmo was invoked to fill the deficiency of Harris based on Marmo's teaching of the use of polymers (i.e., hydroxymethyl cellulose and the like) and/or one or more other water soluble or water swellable polymeric materials (see p. 10, ¶s 0108-0109); (p. 11 ¶ 0115) as well as for the teaching of correcting visual deficiencies such as presbyopia. Applicant argues that Harris is drawn to non-invasive surgical techniques, whereas Marmo uses invasive surgical techniques. This was not persuasive because, nonetheless, both references are drawn to treatment methods in ocular applications and both references are drawn to correcting visual disorders and conditions of the eye. Thus, ample motivation has been supplied based on the combination reference teachings. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See, e.g., In re Kahn, 441 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). ("One of ordinary skill in the art need not see the identical problem addressed in a prior art reference to be motivated to apply its teachings."); In re Linter, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

Accordingly, the 35 U.S.C. 103(a) rejection over Harris and Marmo has been maintained.

Lastly, Applicant argued, "Should the Examiner be minded to further reject claims 1-3, 8, 9, 11-13, 18, 22, and 23 for obviousness, Applicant submits that neither Harris nor Marmo teach, suggest, or provide any motivation to use a combination of hyaluronidase and collagenase. As discussed above, the medicament described by Harris requires hyaluronidase and optionally a number of other corneal softening agents, such as matrix metalloproteinase-1 and matrix metalloproteinase-2 (paragraph [0022] and page 7, Table II, of Harris), and the only reference to collagenase in Harris specifically teaches away from use of that enzyme (paragraph [0087] of Harris). Furthermore, all of the "working" formulations taught in Harris only include hyaluronidase as the singular enzyme in the formulation, see, e.g., the hyaluronidase formulations described in paragraphs [0036], [0037], and [0039] of Harris. Thus, Applicant submits that one skilled in the art, seeking to improve on Harris, might be led to combine hyaluronidase with matrix metalloproteinase-1 or matrix metalloproteinase-2, but would not be led to combine hyaluronidase and collagenase, as presently claimed."

Applicant's arguments have been fully considered but were not found to be persuasive. Applicant argues that "Harris teaches away from the use of the enzyme collagenase". This was not persuasive, because in the paragraph cited by Applicant - paragraph [0087], Harris is only referring to not normally using enzymes which degrade collagen such as collagenase, with respect to soft type contact lenses made of collagenous material and Harris is only making this statement with respect to that particular embodiment only. This is evidenced by Harris's statement at paragraph [0087], stating "Of course, the enzyme or agent used in this embodiment should not normally be one which degrades collagen such as collagenase". Thus, Harris is only referring to possibly avoiding collagenase in terms of soft-type contact lenses. Hence, this argument was not persuasive. Applicant's argument that "neither Harris nor Marmo teach, suggest, or provide any motivation to use a combination of hyaluronidase and collagenase" has been considered and was persuasive. As such, the tertiary reference of Karageozian (USPN 6,610,292) has now been supplied for the teaching that the use of hyaluronidase as well as

alternative enzymes such as collagenase can be used in ocular application treatment methods and thus, was well known to one of ordinary skill in the art. See column 17, lines 29-40. While the combination of both hyaluronidase and collagenase is not explicitly taught, the reference does teach that one of skill in the art would select an appropriate enzyme and its dosage to practice the methods of the invention (column 17, lines 41-51). In addition, the preparation provides for optimal therapeutic effects without causing ocular toxicity. Accordingly, the instant invention would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

--No claims are allowed at this time.

Claims 1-3, 8-14, 16, 18-24 and 51-53 remain rejected.

Claims 4-7, 15, 17, 25-27, 39, 41-46 and 50 remain withdrawn (non-elected invention).

Claims 28-38, 40 and 47-49 have been cancelled.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday-Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached on (571) 272-0623. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/
Primary Examiner, Art Unit 1615

hns

February 23, 2011